Remarks

New claims 27-33 are pending in the application upon entry of the present amendments. The claims are supported in the claims as originally filed, and at least in the specification at paragraphs 57, 60 and 61. No new matter has been added. Applicant thanks the Examiner for withdrawing previous objections and rejections not presently addressed, and addresses the Examiner's rejections in view of the new claims.

The specification has also been amended to correct obvious typographical errors. The amendments do not contain new matter.

Rejections under 35 U.S.C. § 112, second paragraph

Claim 1 is rejected as allegedly being indefinite for reciting "fragment." The rejection is moot in view of new claim 27, and Applicant respectfully requests that this rejection be withdrawn.

Claim 1 is also rejected as allegedly being indefinite for reciting "modulate TRAIL-induced apoptosis." In particular, the Office incorrectly states that "[t]he specification teaches that TRAIL levels are endogenous to any cell [0067]." The cited paragraph relates to pharmaceutical compositions and carriers, and does not support the Examiner's assertions.

As described in the specification, typically, to examine apoptotic activity of a cell, the apoptosis-modulatory polypeptide (i.e., JIK) is endogenously expressed in the cell. To examine whether an agent identified in the first screening step is a modulator of TRAIL-induced apoptosis, the modulating agent is applied to the cells to be tested for apoptosis activity in the presence of TRAIL. If TRAIL-dependent apoptosis activity is altered by addition of the test agent to the assay, the modulating agent identified in the first step is confirmed as a modulator of TRAIL-induced apoptosis. (See, Specification at ¶¶ 57 and 60).

To expedite prosecution without acquiescing to the Examiner's arguments, new claim 27 defines contacting the agent identified in step b) with TRAIL in a cell system wherein JIK is endogenously expressed. Accordingly, claim 27 clearly defines how an agent that

modulates JIK kinase activity is tested for its ability to modulate TRAIL-induced apoptosis, and Applicant respectfully requests that these rejections be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1 and 10-12 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly being nonenabled. Applicant addresses the Examiner's rejections in view of the new claims.

A. Applicant need not Describe All Actual Embodiments

As set forth in the MPEP, "[a] patent need not teach, and preferably omits, what is well known in the art" (MPEP § 2164.01). As discussed below, various assays for analyzing apoptosis activity are well-known in the art and may be employed to monitor the effects of modulating agents on TRAIL-induced apoptosis. Furthermore, because only an enabling disclosure is required, Applicant need not describe all actual embodiments. (MPEP § 2164.02).

As described in the specification, the effects of modulating agents on TRAIL-induced apoptosis can be examined by assaying TRAIL-dependent caspase activation. Figure 2C shows the effect of JIK on caspase activation by TRAIL. Two siRNAs with independent sequences ("1" and "2") were designed to confirm that the screen results are due to target inhibition. As shown in Figure 2C, the increase in TRAIL-dependent caspase activation is distinctly and significantly greater than the increase in TRAIL-independent caspase activation. If TRAIL-dependent apoptosis activity is altered by addition of the test agent to the assay, the modulating agent identified in the first step is confirmed as a modulator of TRAIL-induced apoptosis.

In addition, various assays for analyzing apoptosis activity may be used to monitor the effects of modulating agents identified in the first screening step on TRAIL-mediated apoptosis. For example, the percentage of apoptotic cells induced specifically by TRAIL or a test agent may be calculated. (See, Lichtenstein et al., J. Virol. 76:11329-42 (2002), at page 11332, Materials and Methods; copy attached hereto as Exhibit A). Accordingly, the invention is enabled.

B. The Mechanism Of Action By Which TRAIL Induces Apoptosis Is Not Required For Enablement

Applicant submits that the disclosure in Zhang, Herr I and Herr II is not relevant to the claimed invention. Zhang teaches that JIK could activate the JNK/SAPK pathway, and Herr I and Herr II each discusses JNK/SNPK activity in TRAIL-induced apoptosis. However, whether or not JNK/SNPK is involved in TRAIL-induced apoptosis is irrelevant because the JNK/SNPK pathway is not an element of the claims. Furthermore, as the Examiner correctly noted, "Applicant need not demonstrate how JIK affects TRAIL-induced apoptosis." (*Parker v. Frilette*, 462 F.2d 544, 547; 174 USPQ 321, 324 (CCPA 1972). While the mechanism of action by which TRAIL induces apoptosis is not required for enablement, the binding of TRAIL to death receptors DR4 and DR5 induces apoptosis. (See, Specification at ¶ 2).

C. siRNAs are Tools for Identifying Genes Associated with TRAIL (i.e., JIK)

The Examiner has further mischaracterized the claimed invention by limiting test agents to siRNAs used to identify genes associated with TRAIL. Contrary to the Examiner's assertions, neither the specification nor Aza-Blanc et al. (Molecular Cell 12:627-637 (2003) teaches the requirement for controls using siRNA technology in the claimed methods. Using si-RNA based loss of function screening, the inventors discovered a number of genes (e.g., JIK) that impact TRAIL-induced apoptosis. (See, specification at paragraph 14 and Examples).

Based on the discovery that JIK modulates TRAIL-induced apoptosis, various test agents that modulate JIK may be screened as agents that modulate TRAIL-induced apoptosis. In particular, the claimed methods comprise first identifying an agent that modulates the kinase activity of JIK, and confirming its effect on TRAIL-induced apoptosis activity. Thus, the test agents in the claims are not limited to siRNA used to identify genes associated with TRAIL.

For each of the above reasons, Applicant respectfully submits that the claimed methods are enabled, and requests that this rejection be withdrawn.

Response to Grounds for New Rejections

Claims 1, 10, 11 and 21-26 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. The rejections are moot in view of the canceled claims, and are addressed in view of new claim 27. As previously indicated, claim 27 defines contacting the agent identified in step b) with TRAIL in a cell system wherein JIK is endogenously expressed. Thus, the claims are definite, and Applicant requests that this rejection be withdrawn.

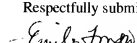
Claim 26 is also rejected under 35 U.S.C. § 112, first paragraph, as allegedly being nonenabled. The rejection is moot in view of canceled claim 26.

Conclusion

In view of the foregoing, Applicant submits that all pending claims in this application are in condition for allowance. The issuance of a formal Notice of Allowance is respectfully requested. If the Examiner believes that a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-812-1539.

In the event that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-1885** referencing docket No. P1111US10.

Respectfully submitted,



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